

### **In the Specification**

***Kindly replace paragraph [0002] with the following:***

#### **Technical Field of the Invention**

[0002] ~~The field of invention~~ Our technology relates to a method of inhibiting angiogenesis or invasion or formation of metastases implicated in numerous pathologies such as cancer, inflammatory diseases, atherosclerosis and pathological angiogenesis of the retina.

***Kindly replace paragraph [0003] with the following:***

#### **Summary of the Invention**

[0003] ~~This invention relates to~~ We provide a method of inhibiting angiogenesis or invasion or formation of metastases in a mammal including administering a therapeutically effective amount of an active agent selected from the group consisting of a protein substance including all or part of a disintegrin domain of an adamalysin or a derivative thereof, a nucleic acid molecule including a polynucleotide sequence coding all or part of the disintegrin domain of an adamalysin or a derivative thereof to the mammal.

***Kindly replace paragraph [0004] with the following:***

[0004] ~~This invention also relates to~~ We also provide methods of treating cancer, inflammatory diseases, atherosclerosis, macular degeneration and psoriasis in mammals including administering a therapeutically effective amount of an active agent selected from the group consisting of a protein substance including all or part of a disintegrin domain of an adamalysin or a derivative thereof and a nucleic acid molecule including a polynucleotide sequence coding all or part of the disintegrin domain of an adamalysin or a derivative thereof to the mammal.

***Kindly replace paragraph [0005] with the following:***

Brief Description of the Drawings

[0005] Other advantages and characteristics of ~~the invention~~ our technology will become clear from the description below pertaining to the preparation AMEP and its *in vitro* and *in vivo* antiangiogenic, anti-invasive and antimetastatic activity, and in which reference will be made to the attached drawings in which:

***Kindly replace paragraph [0016] with the following:***

Detailed Description

[0016] ~~This invention is based on the demonstration of~~ We demonstrate the anti-angiogenic, anti-invasive and anti-metastatic functions of a fragment of a molecule present on human endothelial cells. ~~The invention pertains to~~ We also disclose the use of an adamalysin fragment constituted by all or part of the disintegrin domain. ~~More domain, more particularly, the invention pertains to the~~ use of the disintegrin domain of metargidin (Krättschmar et al., 1996) also referred to below as “AMEP” which stands for “antiangiogenic metargidin peptide”.

***Kindly replace paragraph [0035] with the following:***

[0035] Thus, ~~the invention provides~~ we provide a drug for inhibiting angiogenesis or invasion and/or formation of metastases of an active agent selected from among a protein substance comprising or constituted by all or part of the disintegrin domain of an adamalysin or a derivative thereof, a nucleic acid molecule comprising or constituted by a polynucleotide sequence coding all or part of the disintegrin domain of an adamalysin or a derivative thereof.

***Kindly replace paragraph [0039] with the following:***

[0039] ~~The invention pertains to~~ We provide the disintegrin domain of an adamalysin, more particularly, metargidin and derivatives thereof. Such derivatives constitute functional equivalents having antiangiogenic, anti-invasive and/or antimetastatic properties that one skilled in the art can determine from ~~the teaching of this invention~~ disclosure and, more particularly, from the models and tests presented in the experimental part below. The derivatives can be fragments of truncated form, sequences modified by deletion, addition, suppression or replacement of one or more amino acids. The derivatives can also be fragments corresponding to said derivatives constituted by chemically modified amino acids, these modifications making the derivatives more stable. The invention also pertains to polynucleotide sequences coding for said derivatives.

***Kindly replace paragraph [0040] with the following:***

[0040] ~~The invention,~~ Our technology, thus, also pertains most especially to a nucleic acid molecule comprising a polynucleotide sequence coding all or part of the disintegrin domain of metargidin the sequence in SEQ ID NO. 1 or a derivative thereof. The coding sequence of this domain is constituted by 276 nucleotides (Met-420 to Glu-511).

***Kindly replace paragraph [0045] with the following:***

[0045] ~~This invention,~~ We, thus, ~~offers~~ offer a new method for treating and/or preventing cancer pathologies in general as well as diseases in which angiogenesis contributes to the pathogenesis of the diseases such as inflammatory diseases, psoriasis, atherosclerosis, macular degeneration and the like.

***Kindly replace paragraph [0046] with the following:***

[0046] The active agent is combined in the drugs ~~according to the invention~~ with any pharmaceutically acceptable vehicle known in the art and suitable for the mode of administration employed. Thus, the drugs ~~according to the invention~~ can be administered:

alone, via the systemic, local or oral route or as an implant;

by cell or gene therapy;

in combination with other active principles;

in any pharmaceutical form whatsoever, such as, for example, a nanoparticle form.